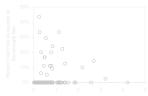
Consumer Advisory for Commercial Fish Maine Department of Human Services Bureau of Health

Why Issue Advice on Commercial Fish?

- · It's the fish most commonly consumed
 - > Women in focus groups asked for information
 - > 80% Maine women of childbearing age eat fish, BUT only 21% report eating any sport-caught fish
 - Higher hair mercury levels (e.g. > 1 ppm) associated with eating commercial fish



Maine Bureau of Health • Environmental Toxicology Program

Consumer Advisory for Commercial Fish Guiding Principles

- · Wanted to follow / support updated US FDA advice
 - > BECAUSE want to avoid confusion & strive for consistency
 - \succ BECAUSE want buy-in from health care providers
- Wanted to redirect fish consumption behavior toward fish lower in mercury
 - > SO, single out "light" vs "white" canned tuna
 - \succ SO, provide limits for general population
- · Keep it simple

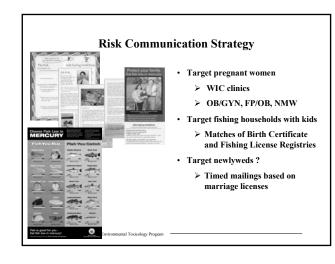
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Consumer Advisory for Commercial Fish



Maine Bureau of Health • Environmental Toxicology Program

Consumer Advisory for Commercial Fish Ocean Fish and Shellfish Striped bass and bluefish Swordfals, shark, litefals and king mackerel All other ocean fish on shellfish White' must have more necrony than "ligh" tuna. Cannel tuna for free owner on the control of the con



Next Steps

- Improve risk communication materials
 - > Redesign brochure for more general population
 - > Mixing and Matching Limits
- Evaluate effectiveness
 - > Surveys of random samples from birth certificate registry
 - ✓ awareness of "safe eating guidelines"
 - √ fish consumption behavior (changes?)
 - \checkmark hair mercury levels

Maine Bureau of Health • Environmental Toxicology Program

Acknowledgements

Funding Support

• U.S. Environmental Protection Agency Office of Water

Collaborators

- Henry Anderson & Laurie Draheim, Wisconsin Division of Family and Community Health
- Sue Stableford, UNE Adult Health Literacy Center
- Doug Campbell, Campbell Creative

Maine Bureau of Health • Environmental Toxicology Program

Methylmercury: Ongoing Research on Toxicology

Kathryn R. Mahaffey, Ph.D. U.S. Environmental Protection Agency, Washington, D.C.



Dietary Sources of Fish & Shellfish Vary Widely Virtually All Contain Methylmercury









Current Toxicology Projects

- Brief note on NRC 2000 Methylmercury Assessment and US EPA's 2001 RfD
- Relation of biomonitoring measures.
- Current reports on blood and hair mercury concentrations in the US
- Reports on adverse cardiac outcomes in adults

Basis for US EPA's RfD for Methylmercury

"Methods and Rationale for Derivation of a Reference Dose for Methylmercury by the US EPA"

Deborah Rice, Rita Schoeny and Kathryn Mahaffey, *in press – Feb 2003* Risk Analysis.

EPA's BMDL for Methylmercury Is Based On:

- Neuropsychological tests that indicate neuropsychological processes involved with a child's ability to learn and process information.
- *Doubling* the risk of scores in a range considered *clinically subnormal*.



Biomarkers of Mercury Exposure and the RfD

Relation of Cord/Fetal Blood Mercury Concentration and Maternal Blood Mercury Concentration

US EPA's Assessment of "Benchmark Dose Lower Bound" for Methylmercury

- BMDL based on a doubling of the prevalence of scores on tests of developmental function in a range recognized as clinically subnormal.
- Both US EPA and NRC utilized a BMDL of approximately 58 ug/L of *cord* blood.
- Dose conversion of *cord* blood [Hg] to *maternal* blood [Hg] assumed to be 1:1.

Comparison of Maternal Blood and Cord Blood Mercury Concentrations

Current risk assessments assume that cord blood and maternal blood [Hg] are equal.

More recent assessments indicate cord blood is, on average, 1.7 times higher in mercury than maternal blood concentrations.

58 ug/L cord blood [Hg] ~ 34 ug/L maternal blood [Hg]

Factors Contributing to Differences in Ratios

- Differences in kinetics of maternal distribution of methylmercury in her body.
- Differences in ratio of cord blood [CH3Hg] to maternal blood [CH3Hg]. Range of means from 2.17 to 1.08. Individual data far more variable. Vahter et al. (2000) reported 5th and 95th percentiles were 0.88 to 3.1.

Dose-Response on the Basis of Blood [Hg]

Cord [Hg] for BMDL: 58 ug/L Maternal [Hg] at 1:1 cord:maternal ratio: 58 ug/L

Maternal [Hg] at 1.7:1 cord:maternal ratio: 34 ug/L

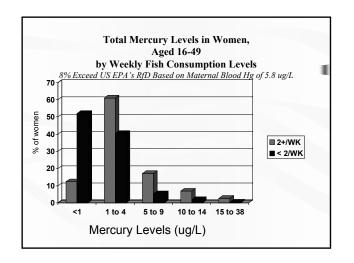
What range of maternal blood concentration are associated with a doubling of the prevalence of neuropsychological deficits?

Blood Mercury Concentrations in the United States Population

NHANES Data

NHANES 1999/2000 - Blood Mercury Women Ages 16 - 49 Years

Blood Hg Ug/L	Number of Subjects	50 th Percentile	90 th Percentile
Women	1709	0.94 (0.73 – 1.15)	4.84 (4.11 – 5.57)



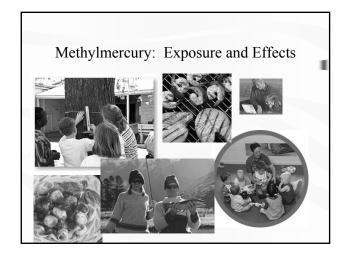
US EPA's Reference Dose for Methylmercury

Effects in Adults

Are there cardiovascular effects of low-dose exposure to methylmercury?

Adult Cardiovascular Effects Association with Mercury Exposures

- Salonen et al. studied 1983 men living in Eastern Finland aged 42 to 60 years (Salonen et al., Circulation 91:645-655, 1955; Atherosclerosis 148:265-263, 2000).
- Report that mercury is a risk factor for coronary and fatal cardiovascular disease.
- Dietary intake of fish and mercury were associated with significantly increased risk of acute myocardial infarction and death from coronary heart disease, cardiovascular disease and any death.
- Men in the highest tertile (2 ppm and higher) hair mercury had a 2-fold (95% Cl 1.2 to 3.1; P=0.005) age- and CHD-adjusted risk of AMI and a 2.9-fold (95% Cl, 1.2 to 6.6; P 0.014) adjust risk of cardiovascular death.
- Carotid intima-media thickness increased with increases in hair mercury concentration. Suggest mercury accumulation in the human body associated with accelerated progress of carotid atherosclerosis (Salonen et al., 2000).



Setting a Methylmercury Reference Dose (RfD) for Adults

Alan H. Stern, Dr.P.H., DABT

Division of Science, Research & Technology New Jersey Department of Environmental Protection

Trenton NJ

- However, for MeHg, the sensitive population is well characterized
 - women of childbearing age, pregnant women, young children
- Individuals have reasonable control over exposure
 - consumption of fish with lower Hg conc.

The Two-Tiered Advisory Structure

- The policy of the U.S. EPA is to derive a single RfD per chemical
 - based on goal of protecting most sensitive group
 - generally, members of the sensitive group are not known, or cannot control their exposure (e.g., air, drinking water)
 - therefore, protection of sensitives results in overprotection of general population

- In principle, this lends itself to a two-tiered advisory structure
 - sensitive population and general population
 - general population is not overly protected and has less potential limitations on obtaining nutritional value from fish
 - sensitive population is protected at more stringent level

- Two-tiered approach based on two RfDs
 - neuro-developmental effects for sensitive population
 - current RfD
 - neurological effects for general population
 - paraesthesia predictive and protective for progression of neurological effects
 - · old RfD
 - from Iraq and Minimata

- Currently, 12-13 states follow such a two-tiered approach
- Appropriateness of approach is predicated on assumption:

$$Rfd_{gen} > RfD_{sens}$$

- Current RfD = 0.1 ug/kg/day Old RfD = 0.3 ug/kg/day
 - difference is small, but significant for fish advisories

- Is assumption that Rfd_{gen} > RfD_{sens} correct?
- NAS/NRC report highlights several areas of uncertainty for general ("adult") RfD
 - cardiovascular effects
 - immunotoxic effects

- Salonen et al. (2000)
 - middle aged men in Finland
 - 4 year follow-up assessing hair Hg, and atherosclerosis progression
 - · ultrasound determination of carotid artery thickness
 - after adjustment for co-variates, men in upper quintile of hair Hg (2.8 ppm) had 40% increase in arterial wall thickness

EPA Sponsored Effort

- Contract with State of NJ (in process)
 - PI Dr. Alan H. Stern
 - Co-PI Dr. Andy E. Smith, ME
- State toxicologists, epidemiologists, risk assessors
 - 6-7 states represented
- independent consultants in statistics and cardio-epi
- 12-18 months duration

Summary of reported findings for cardiovascular endpoints for MeHg

- Salonen et al. (1995)
 - middle aged Finnish men
 - mean hair Hg = 1.92 ppm
 - approx. 2.3 times NJ general pop. mean
 - for hair Hg >2 ppm, adjusted RR for

AMI, CHD, and CVD = 1.7-2.1

• in NJ ~20% of general population >2 ppm

Implications for Hg Fish Advisory Structure

- RfD $_{general} > RfD$ $_{sensitive}$
 - retain two tiered advisory structure
 - · currently only separated by 0.2 ug/kg/day
 - if RfD _{general} decreases by 0.1 ug/kg/day will difference in advisories be significant?
- RfD $_{general}$ < RfD $_{sensitive}$
 - one advisory?
 - · does cardiovascular endpoint apply to women?

Occurrence of PBDE Flame Retardants in Fish



Robert C. Hale Virginia Institute of Marine Science

VIMS: M. La Guardia, E. Harvey, M. Mainor, E. Bush, M. Gaylor,
S. Ciparis, M. Jacobs & D. Luellen

<u>Virginia Dept. of Environmental Quality</u>: J. Gregory, A. Barron, G. Darkwah & R. Browder



Brominated Flame Retardants (BFRs)

 Chemicals added (up to 30% by weight) to reduce fire hazard associated with our wide use of flammable polymers & textiles



BFR use saves:
Lives
Property
Environmental damage

Brominated Flame Retardants (BFRs) Differ in Structure



Hexabromocyclododecane (HBCD)



Polybrominated Biphenyls (PBBs)



Tetrabromobisphenol-A (TBBP-A)



Polybrominated diphenyl Ethers (PBDEs)

Once upon a time... we stopped using PBBs



Learned that their structural similarity to PCBs and other persistent, bioaccumulative & toxic (PBT) chemicals was problematic



PBBs accidentally introduced into MI livestock feed in 1973

Destroyed large numbers of animals MI residents still carry PBB burdens.

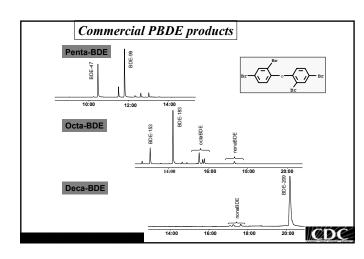


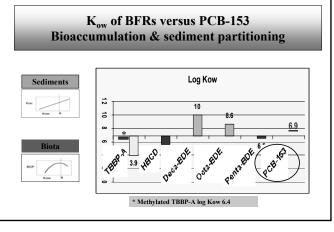
Shhhh....Apparently we shifted to PBDEs instead...



3 Commercial PBDE Mixes

3 Commercial PDDE Mixes							
Br _x	Uses Nondispersive?	1999 Demand American % of global use					
Deca-BDE	Thermoplastics & textiles	24,300 MT 44.3 %					
Octa-BDE	ABS plastics	1375 MT 35.9 %					
Penta-BDE	Polyurethane foam	8290 MT 97.5 %!!!					





PBDEs: General Environmental Concerns

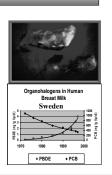


- · Resistant to environmental degradation
- Long-range transport POP?
 - Less brominated congeners atm transport
- Accumulation in fish is a major pathway for human exposure – as per PCBs
- · PBDEs accumulate in lipid-rich tissues
 - Penta-BDE mix > Octa-BDE > Deca- BDE
 - · BDE-47 bioconcentration > PCBs



PBDE Research: Europeans More Active

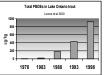
- Reporting PBDEs in fish, mostly less brominated, since 1980's
- Detected even in remote areas
 - Arctic & deep ocean
- Rising in human breast milk
- E.U. Ban of Penta- mix in 2003
- Concern turning to Deca-BDE
 - Debromination?

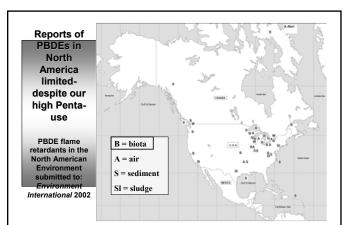


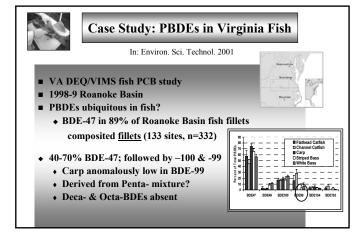
Overview: PBDEs in U.S.

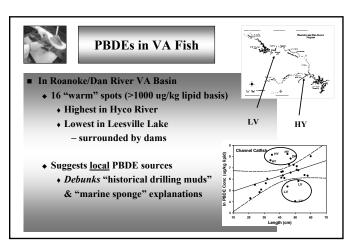


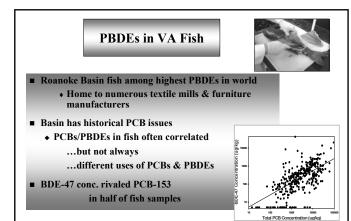
- No specific U.S. regulations or widespread monitoring
- Detected in U.S. aquatic environment in 1987
 - EPA: Atlantic dolphin mortality event
 - Tetras Hexa PBDEs ~ 200 ug/kg (lipid)
- Marine mammals high accumulators
 - Indigenous populations at future risk?
 - San Fran Harbor seal 8325 ug/kg
 65-fold increase from 1988-2000
- · U.S. fish increasing over time
 - Penta-like congeners most common

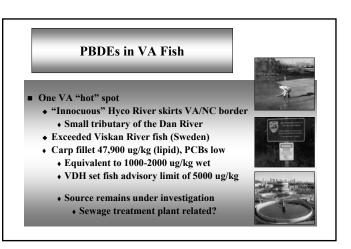


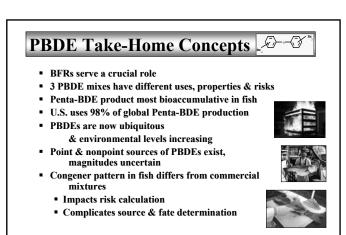


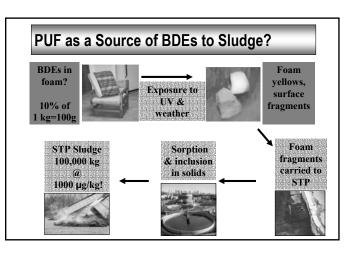












PBDEs: Toxicology and Human Exposure

Linda S. Birnbaum, Ph.D., D.A.B.T. NHEERL/ORD/US EPA

Major Industrial Products (~67 metric tons/year)

- DBDE largest volume (75% in EU)
 - 97% DBDE; 3% NBDE
 - Polymers, electronic equipment>textiles
- OBDF
 - 6%HxBDE; 42%HpBDE; 36% OBDE; 13%NBDE;
 2%DBDE multiple congeners (unclear if any PeRDE)
 - Polymers, esp. office equipment
- PeBDE
 - Textiles esp. polyurethane foams (up to 30%)
 - Recommended ban in EU(no production/only import)
 - Mainly PeBDE+TeBDE, some HxBDE

PBDEs in Biotic and Abiotic Samples

- Air: 47>99>100>153=154
- Sediment: 99>47 (pattern reflects commercial PeBDE); also some nona and deca
- Sewage Sludge: 1-3mg/kg in US; pattern ~ RUFs
 Point sources (~DBDE) --->0.1-5 mg/kg
- Biota: 47>99=100 except if near manufacturing site (pattern does NOT reflect commercial PBDEs)
- Invertebrates<Fish<<marine mammals

PBDEs (con) Ecotoxicity

- PeBDE>>OBDE>DBDE
 - Highly toxic to invertebrates (Larval development, LOECs in low μg/l range)
- DBDE/OBDE
 - May be low risk to surface water organism and top predators
 - Concern for waste water, sediment, and soil organisms
 - CONCERNS:
 - · Presence of lower brominated congeners in OBDE
 - · Photolytic and/or anaerobic debromination
 - · Formation of PBDDs/PBDFs

Mammalian Toxicity of PBDEs

- Hepatotoxic
- Enzyme Induction
- DBDE hepatocarcinogen (high dose)

Neurotoxic Effects

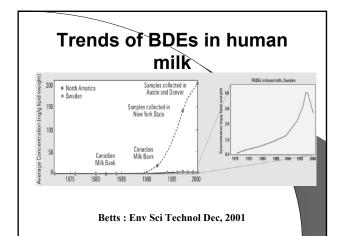
- Developmental Neurotoxicants
 - Perinatal; neonatal pnd10 in mice
 - 47,99,153,209
 - Spontaneous behavior (mice)/hyperactivity
 - Permanent changes in brain function
- Developmental exposure -→Increased susceptibility of adults exposed to low doses of PBDEs
- In vitro changes in signalling pathways

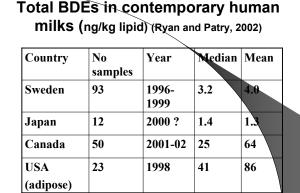
Endocrine Disrupting Effects

- AhR Effects
 - Relevance for commercial BFRs?
 - · combustion can produce PBDDs/PBDFs
 - Recently found in human adipose tissue
- Thyroid
 - OH-PBDE metabolites bind to transthyretin
 - Parent PBDEs Effects on T4 seen in vivo
 - induction of UDP-glucuronyl transferase
 - Rats and mice; body burdens as low as 0.8 mg/kg
- Estrogenic
 - OH-PBDEs
 - Sulfotransferase inhibition (mostly in vitro)

Pharmacokinetics of PBDEs

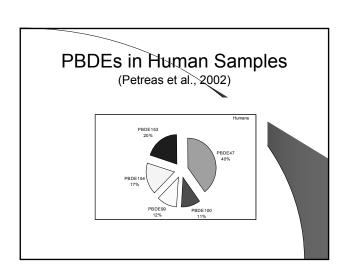
- Absorption DBDE is poorly absorbed
- Distribution lipid binding is important
 - Fat: 47>99>>>209
 - Liver: covalent binding from 99,209
- Metabolism hydroxylation, debromination, O-methylation
- Excretion feces is major route

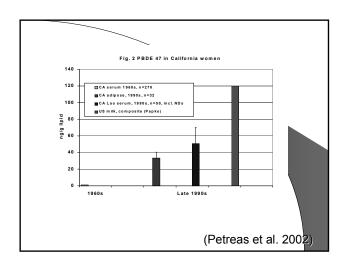


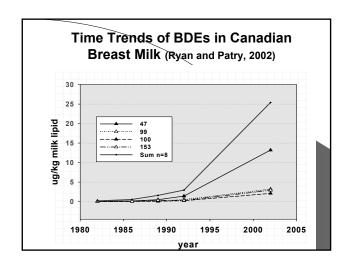


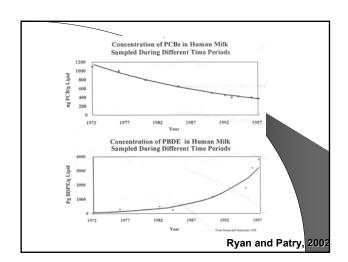
Total BDEs (n=7) in Canadian individual human milks (ng/kg lipid) (Ryan and Patry, 2002)

Location	No samples	Year	Median	Mean
Canada	72	1992	3.0	15
Canada	50	2002	25	64









PBDEs in Human Samples

- Pattern of congeners is different from commercial mixtures (and food)
 - 47>99 in US and Europe(others: 100,153,183, 2093)
 - In Japanese, 99 and 153>47
- Large interindividual differences
- Increasing time trends levels doubling every 2-5 years
- PBDEs and PCBs levels are not correlated
 - In most samples today, PCBs>PBDEs
- different sources and/or time sequence

Time Trends of Biotic Levels

- Rapid increases from 70s thru 90s
- Maybe slight decrease in Sweden
 - Ban on use of PeBDE?
- Levels still increasing in America
 - Continued use of PeBDE?
- ARE LEVELS HIGH ENOUGH TO SEE EFFECTS??? NEED MORE TOX DATA!

What next?

- More systematic human and environmental monitoring
- More information on fate and transport are commercial products breaking down? And into what?
- More tox data Focus on congeners present in people and wildlife, NOT commercial products since they are altered in the environment

Polybrominated Diphenyl Ethers (BDEs)

Khizar Wasti, Ph.D.
Virginia Department of Health



Phone: (804) 786-1763 FAX: (804) 786-9510

E-mail: kwasti@vdh.state.va.us http://www.vdh.state.va.us/hhcontrol

Toxicity of Deca-BDE

- ◆ The acute toxicity in experimental animals is low; oral LD50 in rats is >5mg/kg.
- No adverse effects were noted in rats fed at doses of up to 800 mg/kg BW for 30 days
- No evidence of carcinogenic, reproductive, teratogenic, or mutagenic effects
- Epidemiological studies in occupationally exposed workers did not indicate any symptoms attributable to BDEs exposure
- ◆ Oral RfD 0.01 mg/kg/day



Toxicity of Octa-BDE

- Low acute oral toxicity; LD50 in rats >5-28 g/kg
- Low chronic toxicity
- Teratogenicity-at doses of 25 and 50 mg/kg BW, resorptions or delayed ossification of different bones and fetal malformations were noted in rats. These changes were not seen at 15 mg/kg or less. In rabbits there was no teratogenicity, but fetotoxicity was seen at maternally toxic dose of 15 mg/kg. A no-effect level was 2.5 mg/kg
- Mutagenicity- negative
- Carcinogenicity- no data available
- IRIS Data Base- Oral RfD 0.003 mg/kg/day



Toxicity of Penta-BDE

- Low acute oral toxicity; LD50 in rats 6-7 g/kg
- Rats given diet containing 100 mg/kg for 90 days showed no clinical effects
- Not found to be mutagenic
- No data on carcinogenicity
- IRIS Data Base- Oral RfD 0.002 mg/kg/day



Toxicity of Tetra-BDE

- Virtually no human or animal data are available
- Toxicity may be similar to commercial Penta-BDE since it contains significant amount of tetra-isomer



Derivation of Allowable BDE Levels in Fish

Based on oral RfD,

Penta-isomer 0.002 mg/kg/day
Octa- isomer 0.003 mg/kg/day
Deca-isomer 0.01 mg/kg/day



BDE Task Force

- Virginia Department of Health
- Virginia Department of Environmental Quality
- Virginia Department of Game and Inland Fisheries
- Virginia Institute of Marine Sciences
- North Carolina Department of Health and Human Services
- North Carolina Department of the Environment
- U.S. Environmental Protection Agency
- Centers for Disease Control and Prevention



Selection of RfD for Risk Assessment

- Use the RfD value for penta-isomer, 0.002 mg/kg/day
- EPA suggested an interim RfD for tetra-isomer, 0.001 mg/kg/day. This RfD was based on the assumption that the tetra-BDE was twice as toxic as the penta-isomer

Derivation of Acceptable Concentration in Fish

 $C = RfD \times BW \times T$

MS x NM

C = acceptable concentration

RfD= reference dose

BW = average adult weight (70 kg)

T = Time period, 30 days/month

MS = meal size, 8-ounce or 0.227 kg

NM = number of meals/month, 2



Allowable Concentration of BDEs in Fish for Two Meals per Month

0.001 mg/kg/day x 70 kg x 30 days/month

0.227 kg/meal x 2 meals/month

= 4.62 ~ 5.0 mg/kg or parts per million (ppm)



Number of Allowable Fish Meals per Month at Various BDE levels

Cond	entration	# of Meals per month
1	ppm	9.3
1.47	ppm	6.3
2	ppm	4.6
3	ppm	3.1
4	ppm	2.3
5	ppm	1.9
9	ppm	1
10	ppm	0.9
		₩DH:

Guidance for Issuing Fish Consumption Advisories

BDE concentrations

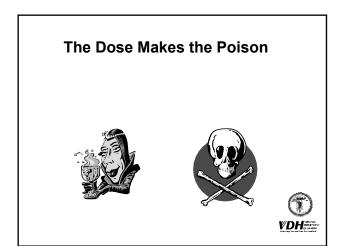
Below 5 ppm No Advisory

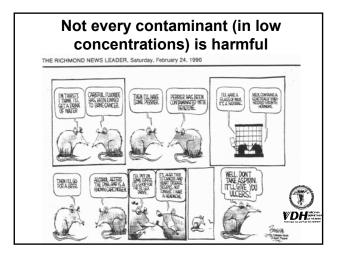
• 5 ppm - < 10 ppm Two 8-oz meals/month

• >10 ppm No consumption

Since reproductive or developmental effects of tetra-BDE have not yet been evaluated, it would be prudent for pregnant women, nursing mothers, and young children to avoid consumption of fish contaminated with BDEs above 5 ppm

VDH



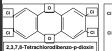


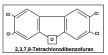
EMERGING SCIENCE OF THE DIOXIN REASSESSMENT



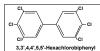
Dwain Winters Director Dioxin Policy Project Office of Pollution Prevention and Toxics US EPA 202 566 1977 winters.dwain@epa.gov

Dioxin-Like Compounds





Furans



Dioxins 75 congeners 7 toxic

7 toxic 2,3,7,8-TCDD 1,2,3,7,8-PeCDD 1,2,3,4,7,8-HxCDD 1,2,3,6,7,8-HxCDD 1,2,3,6,7,8,9-HxCDD 1,2,3,4,6,7,8-HyCDD 1,2,3,4,6,7,8-PCDD 135 congeners 10 toxic 2,3,7,8-TCDF 1,2,3,7,8-PeCDF

2,3,7,8-TCDF 1,2,3,7,8-PeCDF 2,3,4,7,8-PeCDF 1,2,3,4,7,8-HxCDF 1,2,3,6,7,8-HxCDF 1,2,3,7,8,9-HxCDF 1,2,3,4,6,7,8-HxCDF 1,2,3,4,6,7,8-HpCDF 1,2,3,4,6,7,8,9-CDDF 1,2,3,4,6,7,8,9-CDDF 209 congeners 12 toxic

3,3',4,4'-TeCB 3,3',4,4',5-PeCB 3,3',4,4',5,5'-HxCB Plus 9 others

Toxic Equivalency (TEQ)

- Fundamental to evaluation of this group of compounds
- Based on inspection of multiple endpoints and/or receptor binding (WHO criteria)
- Reassessment Chapter Summarizes Scientific Support
- WHO₉₈ internationally accepted

Five Compounds Make up About 80% of the Total TEQ in Human Tissue

- •Four of 17 Toxic CDD/CDF Congeners
- •One of the 12 toxic PCBs
 - > 2,3,7,8-TCDD
 - > 1,2,3,7,8-PCDD
 - > 1,2,3,6,7,8-HxCDD
 - > 2.3.4.7.8-PCDF
 - > PCB 126

Current Dioxin Exposure/Body Burdens

- > ~ 1 PG TEQ/Kg/Day (PCDDs/PCDFs/PCBs)
- > Possible Higher Intake Populations
 - Nursing infants
 - Fatty Diet
 - Some subsistence fishermen and farmers in proximity to contamination

Body Burden Best Dose Metric (Ng/Kg BW)

- Accounts for differences in half-life
- Results in strong agreement between human and animal data
- Adopted by WHO, EC, HHS

Dioxins and Human Carcinogenicity

2,3,7,8-TCDD

Carcinogenic to humans

Other dioxin-like compounds

Likely to be carcinogenic

Complex Environmental -**Mixtures**

Likely to be carcinogenic

- Based on: ◆ Unequivocal animal carcinogen
 - ◆ Limited human information (epidemiological/other)
 - ◆ Mechanistic plausibility

Cancer potency increasingly focusing on human studies

Note: (IARC) classified TCDD as a Category 1, "Known" human carcinogen. DHHS 9th Report on Carcinogens (ROC) the same

Quantitative estimate of cancer risk

- Cancer slope factor is based primarily on recently published analyses of human studies and is revised upward by a factor of ~6 over the 1985 EPA value based on 1978 study in rats
- Cancer risks to the general population may exceed 10-3 (1 in 1,000) from background (dietary) exposure but are likely to be less and may even be zero for some individuals

Non-cancer Toxicants in Animals and Humans

- → Developmental Toxicity Targets:
 - > Developing Immune System
 - > Developing Nervous System
 - > Developing Reproductive System
- → Immunotoxicity
- → Endocrine Effects
- → Chloracne
- → Others

Body Burdens Associated With Non-Cancer Effects

- Auverse Effects	ng/ng	MOE
Developmental neurotoxicity:	22	4
> Developmental/reproductive toxic	city: 0.7 - 42	0.1 - 8
Developmental immunotoxicity:	50	10
> Adult immunotoxicity:	1.6 - 12	0.3 - 2
> Endometriosis:	22	4
→ Biochemical Effects		
> CYP1A1 Induction:	0.6 - 33	0.1 - 7
> CYP1A2 Induction:	2.1 - 83	0.4 - 17

Να/Κα

MOE*

*MOE = effect level / current average U.S. background body burdens of 5 Ng/Kg

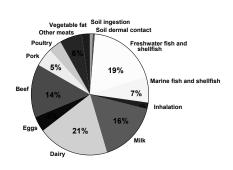
Characterization of Non-Cancer Effects

- Identification of non-cancer effects in animals and human are sufficient to generate a similar level of concern to cancer
- Adverse non-cancer effects have been observed in animal and humans within 10 times background exposure.
- > It is likely that part of the general population is at, or near, exposure levels where adverse effects can be anticipated
- > EPA will rely on MOE rather than RfD as the risk descriptor for dioxin non-cancer risk

U.S. Adult Average Daily Intake of CDDs/CDFs/ Dioxin - Like PCBs

65 pg TEQ_{DFP}-WHO₉₈/day

Advance Effects



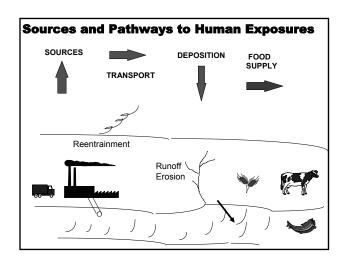
U.S. Levels in Food CDD/CDF/PCB TEQ_{WHO98} (whole weight basis) 0.18 ± 0.11 Range = 0.11 - 0.95 n=78 0.28 ± 0.28 n = 78 **0.012** Lorber et al. (1997b) Poultry, ppt Ferrario et al. (1997) n=78 0.068 ± 0.070 Range = 0.03 - 0.43 Milk, ppt n=8 composites 0.018 n = 8 composites 0.0088 Lorber et al. (1998b) Dairy, ppt = 8 composites Based on data from Lorber et al. (1998b) 0.18 orber et al. (1998b) Mes et al. (1991)

		Consumption Rate		CDD/CDF TEQ Conc.	CDD/CDF TEQ Intake
Fish Class	Species	(g/day)	N	(Pg/g fresh wt.)	(pg/day)
Estuarine Finf	Flounder (e)(f)	0.58	3	1.8	1.0
	Rockfish/Striped Bass (d)	0.043	26	1.2	0.052
	Salmon (d)	0.042	39	0.57	0.024
	Mullet (a)	0.034	2	0.068	0.0023
	Other Flatfish	0.39	0		
	Perch	0.39 0.19 0.13 0.12	ŏ		
	Croaker Herring	0.13	ō		
	Anchovy Smelts	0.042 0.0074	0		
	Eel	0.0038	ō		
	Sturgeon Total Other*	0.00017 0.88	0	1.3	1.1
Freshwater Finfish	Catfish-farmed (b,d,h)	0.90	30	2.0	1.8
	Trout-farmed (e,h)	0.41	6	1.9	0.78
	Perch (e) (walleye)	0.17	3	1.2	0.20
	Carp (e)	0.14	4	1.2	0.17
	Pike (e) (pickerel)	0.035	3	0.49	0.017
	Salmon (d) Other	0.00083	39	0.57	0.00047
	Whitefish	0.012 0.0012			
	Cisco Smelts.	0.00050	ŏ		
	Rainbow Sturgeon	0.00017 0.014	0		
	Total Other*		0	1.3	0.018
Total Freshwater/Est. Finfish		2.0	116	1.6	5.3
Freshwater/Estuarine Shellfish	Shrimp (b,c)	2.0	119	0.080	0.16
	Crab Average (i)	0.30	33	0.37	0.11
	Oyster Average (i)	0.15	18	0.47	0.070
	Scallop (d)	0.0011	.11	0.16	0.00018
	Crayfish (i)	0.0090	25	0.30	0.0027
	Other	0.014	L		T
	Clam Snails	0.0017	8		
	Total Other**	0.0157	0	0.43	0.0068
Total Freshwater/Est. Shellfish		2.5	106	0.14	0.35
Unknown Freshwater/Est. Species	Fish***	0.14	0	1.3	0.18
Total Fresh./Est. Fish	1	5.9	222	1.0	5.8

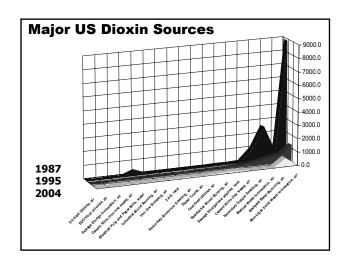
Fish Class	Species	Consumption Rate (g/day)	N	CDD/CDF TEQ Conc. (Pg/g fresh wt.)	CDD/CDF TEQ Intake (pg/day)
Marine Finfish	Tuna (c)	3.1	16	0.060	0.19
	Cod (c) Salmon (d)	1.4	18	0.15	0.21
	Pollack (d)	0.25	19	0.22	0.055
	Mackerel (a)	0.11	1	0.95	0.10
	Porgy Haddock Haddock Haddock Haddock Haddock Perch Sardine See Bass Total Other***	0.31 0.26 0.17 0.13 0.12 0.10 0.98 0.098 0.073 0.045 0.035 0.035 0.032 0.0066 0.0046 0.0011	000000000000000000000000000000000000000	0.39	0.72
Total Marine Finfish		8.0	93	0.25	2.0
Marine Shellfish	Scallop (d) Lobster (d) Crab (d)	0.19 0.19 0.16	11 16 38	0.16 0.26 0.36	0.030 0.049 0.058
	Other Clams Mussels Conch Snails Total Other****	0.70 0.070 0.0021 0.0017 0.77	0	0.26	0.20
Total Marine Shellfish		1.3	65	0.26	0.34
Unknown Marine Species	Seafood (g)*** Fish***	0.080	0	0.39	0.031
Total Marine Fish	1 601	9.6	158	0.26	2.5
TOTAL FISH	1	15.5	292(i)	0.53	8.3

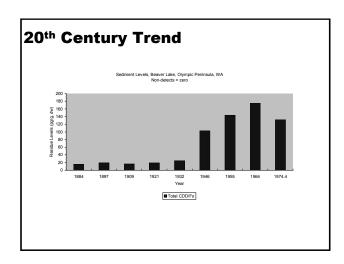
Pathways and Sources of Human Exposures

- Pathways:
 - → Ingestion of soil, meats, dairy products, fish
 - → Inhalation of vapors and particulates
 - → Dermal contact with soil
- Sources:
 - → Combustion
 - → Metal Smelting, Refining, Processing
 - → Chemical manufacturing
 - → Biological and Photochemical Processes
 - → Reservoir sources



United States - Sept. 2000 Grait	WHO SHAPE	WHAT IN	- 1220
Municipal Solid Waste Incineration, air	8877.0	1250.0	38%
Backyard Barrel Burning, air	604.0	628.0	19%
Medical Waste Incineration, air	2590.0	488.0	15%
Secondary Copper Smelting, air	983.0	271.0	8%
Cement Kilns (haz waste), air	117.8	156.1	5%
Sewage Sludge/land applied, land	76.6	76.6	2%
Residential Wood Burning, air	89.6	62.8	2%
Coal-fired Utilities, air	50.8	60.1	2%
Diesel Trucks, air	27.8	35.5	1%
Secondary Aluminum Smelting, air	16.3	29.1	1%
2.4-D. land	33.4	28.9	1%
Iron Ore Sintering, air	32.7	28.0	1%
Industrial Wood Burning, air	26.4	27.6	1%
Bleached Pulp and Paper Mills, water	356.0	19.5	1%
Cement Kilns (non-haz waste), air	13.7	17.8	1%
Sewage Sludge Incineration, air	6.1	14.8	0%
EDC/Vinyl chloride, air	NA.	11.2	0%
Oil-fired Utilities, air	17.8	10.7	0%
Crematoria, air	5.5	9.1	0%
Unleaded Gasoline, air	3.6	5.9	0%
Hazardous Waste Incineration, air	5.0	5.8	0%
Lightweight ag kilns, haz waste.air	2.4	3.3	0%
Kraft Black Liguor Boilers, air	2.0	2.3	0%
	2.0	2.2	0%
Petrol Refine Catalyst Reg., air Leaded Gasoline, air	37.5	2.0	0%
	12	1.7	0%
Secondary Lead Smelting, air			
Paper Mill Sludge, land	14.1	1.4	0%
Cigarette Smoke, air	1.0	0.8	0%
EDC/Vinyl chloride, land	NA	0.7	0%
Primary Copper, air	0.5	0.5	0%
EDC/Vinyl chloride, water	NA.	0.4	0%
Boilers/industrial furnaces	0.8	0.4	0%
Tire Combustion, air	0.1	0.1	0%
Drum Reclamation, air	0.1	0.1	0%
TOTALS	13,995	3,252	
Percent Reduction from 1987	1	77%	1





Poorly Characterized Sources

Secondary steel electric arc furnaces

Coke production

Ceramic manufacturingClay processing

• Ferrous and non-ferrous foundries

Asphalt mixing plants

Primary magnesium

Frimary magnesiur

• TiO₂

Wood stoves

Forest fires

Brush fires

· Range fires

· Ag burning

· Landfill fires

· Structural fires

· Landfill flares

· Rural soil erosion to water

· Urban runoff to surface water

• Utility poles and storage yards

· Landfill fugitive emissions

• Transformer storage yards

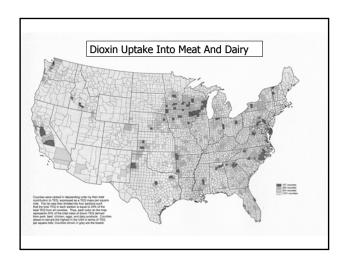
Reservoir Sources

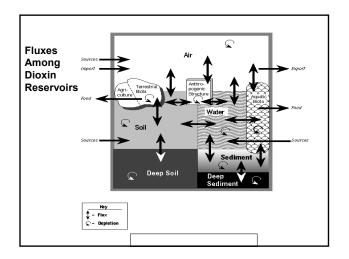
Old releases of dioxins that are temporarily stored in environmental compartments to later be reintroduced into the circulating environment:

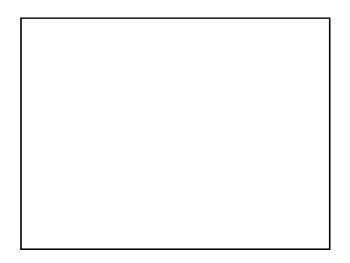
- Soil
- Sediment
- Biota
- Materials

Reservoirs contribute as much as 50% to general population exposure.



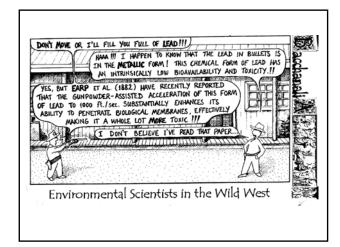


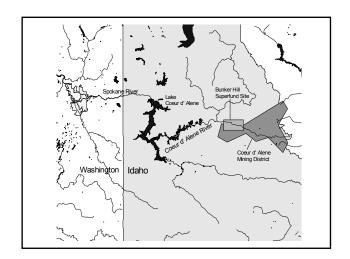


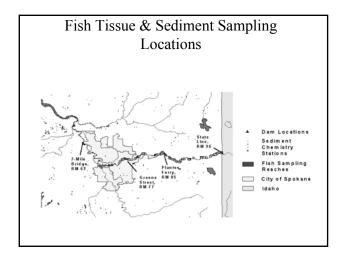


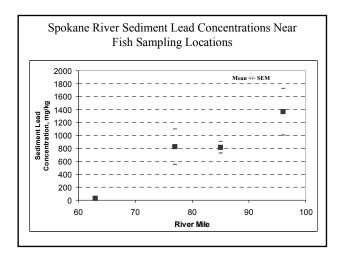
Application of the Lead IEUBK Model to Assess Spokane River Fish Consumption Health Risks

Lon Kissinger, U.S. EPA Region 10









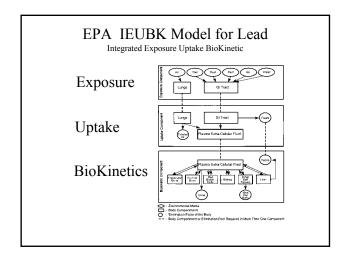
Lead Risk Assessment

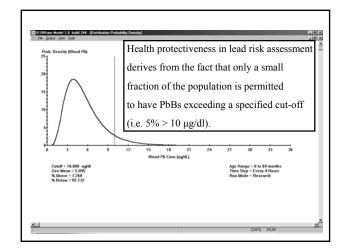
- Based on internal measure of exposure, blood lead level (PbB)
- Risks assessed by comparing predicted population PbB values to PbB values associated with health effects.
- This approach integrates lead risks for all exposure routes.

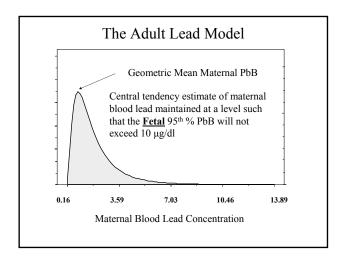
	Dose-Response –	→ ?Thr	eshold
	Observed Effect		ren Adults Lead µg/dl
	Death	≥125	?
	Neurological		
	Encephalopathy	70	100
Sub-clinical	Peripheral Neuropathy	40	40
\longrightarrow	Central Nervous System		
	↓ Hearing		10
	↓ Cognitive IQ	10	-
	↓ Psychomotor Function_	10	-
	↓ Birth weight/ Term length	10	-
	Anemia	20	80
	↓ Heme synthesis	10	10
	Renal nephropathy	40	40
	Hypertension		25
	↓ Vitamin D	< 30	
	↓ Sperm count & function		40
	Adapted from Casserett & Doull's TOXICOLOG	Y and ATSDR	

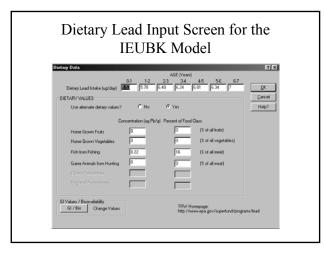
Models Used to Assess Lead Health Risks

- Models used:
 - Risks to children: ages 0 to 84 months assessed using the Integrated Exposure Uptake Biokinetic Model (IEUBK)
 - Risks to developing fetus: determined using the adult lead model.
- Information at: EPA's Lead Technical Review Workgroup: http://www.epa.gov/superfund/programs/lead/









Key IEUBK Model Parameters

- Fraction of meat consumption that consists of locally caught fish.
- Concentration of lead in fish tissue.
- Lead concentration and intake rates for other media (e.g. water, soil, house dust)

Fraction of Meat Consisting of Spokane River Fish: Fish Consumption Rate

- What childen's fish consumption rate to use?
- Identified populations included:
 - Recreational anglers
 - Laotians
 - Russian immigrants that consumed fish cakes prepared by grinding fish after removal of head & spine.
- Problem: No quantitative information

Fraction of Meat Consisting of Locally Caught Fish: Fish Consumption Rate (continued)

- Opted to use tribal fish consumption rates for children age 0 to 72 months.
- Rates taken from the Columbia River Intertribal Fish Commission Fish Consumption Study (EPA, 2002).
- 65th percentile consumption rate of 16.2 g/day was used as a health protective central tendency estimate.

Fraction of Meat Consisting of Locally Caught Fish: Meat Consumption

IEUBK model variable: meat_all(t)

 Age (months)
 g/day

 12-24
 87

 25-36
 96

 37-48
 102

 49-60
 107

 61-72
 112

 72-84
 121

Avg. for children 0-72 months = 101 g/day, therefore, a fish consumption rate of 16.2 g/day is 16% of total meat consumption

Fish Species Assayed for Lead



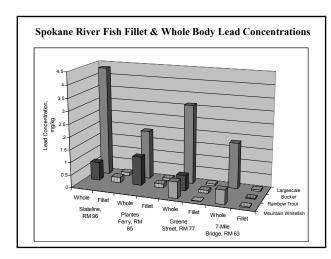




Largescale Sucker



Rainbow Trout

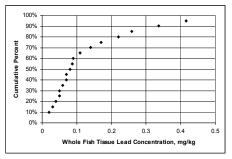


Comparison of Spokane River Average Whole Fish Lead Levels with National Values (mg/kg)

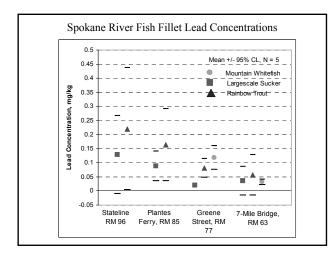
0.168				
	2			

C.J. Schmitt and W.G. Brumbaugh, 1990. National Contaminant Biomonitoring Program: Concentrations of Arsenic, Cadmium, Copper, Lead, Mercury, Selenium, and Zinc in U.S. Freshwater Fish, 1976-1984. Archives of Environmental Contamination and Toxicology. 19:731-747.

Distribution of Lead Concentrations in Whole Fish

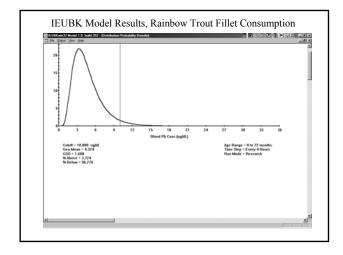


C.J. Schmitt and W.G. Brumbaugh, 1990



Selected IEUBK Model Parameters

- Stateline trout fillet lead concentration of 0.22 mg/kg.
- Soil concentration of 230 mg/kg.
- All other parameters set at model defaults.



PbBs Resulting from Consumption of Whole Fish

	Max Observed Concentration	% > 10 Micrograms
Species	(mg/kg)	<u>per dl</u>
Largescale	4.34	62%
Sucker		
Rainbow Trout	1.14	15%
Mountain Whitefish	0.56	6%

Computing Pb Fish Fillet Consumption Limits

In order to run the IEUBK model, fish meals are converted to fish intake as % of meat intake:

(N meals per month X 8 oz.) / 30 days $\,X\,$ 28.349 g / oz.

IEUBK daily meat intake in g / day

Comparison of Children's and Adult Fillet Meal Limits

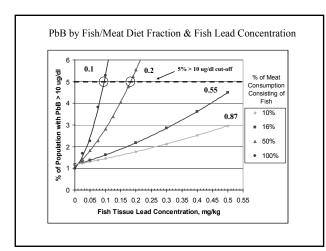
8 oz. Meals per Month

	IEUBK	ALM
Species	Children	Adults
Rainbow Trout	4	8
Largescale Sucker	7	14
Mountain Whitefish	13	52

PCB Based Spokane River Fish Consumption Limits

Allowable 8 oz. Meals

	PCB Conc., ppb		per Y	ear
Species	Avg.	High End	Avg.	High End
Rainbow	880	1312	2.6	1.7
Trout				
Largescale	148	182	15.2	12.4
Sucker				



Issues/Model Improvements to consider:

- Consider altering the model to accept more population specific dietary information.
- Evaluate how the model does with subsistence consumption.
- Are there differences in bioavailability of lead found in bone/cartilage vs. muscle tissue?
- Change consumption rate data entry from fish as % of meat consumption to g/day.

Acknowledgements

- Nancy Beck, U.S. OMB
- Steven Box, USGS
- Robert Duff, WA Dept. of Health/ATSDR
- Art Johnson, WA Dept. of Ecology
- Mike LaScuola, Spokane Regional Health District
- Terry Maret, USGS
- John Roland, WA Dept. of Ecology
- Marc Stifelman, U.S. EPA

Equations for the Adult Lead Model

Intake of Lead from Soil and Fish

 $PbB_{adult, central} = PbB_{adult, 0} +$

BKSF x (PbS x IR_s x AF_s x EF_s + PbF x IR_F x AF_F x EF_F) / AT

Equations for the Adult Lead Model (continued)

What maternal blood lead level will be

protective of the fetus?

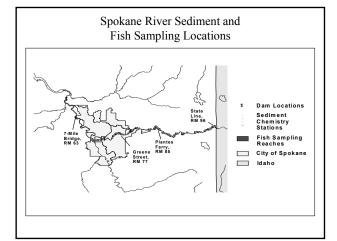
PbB_{fetal, 0.95 goal} = PbB adult, central goal x GSD^{1.645} x R_{fetal/maternal}

PbB _{adult, central goal} = $(PbB_{fetal, 0.95 \text{ goal}}) / (GSD^{1.645} \times R_{fetal/maternal})$

Finally, is PbB_{adult, central} < PbB _{adult, central goal}?

Supplement

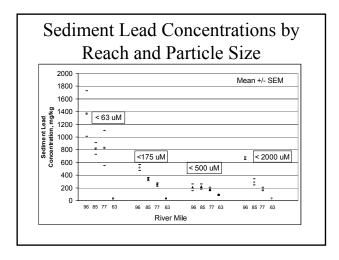
 The following slides were not presented at the forum but were provided by the author for inclusion in the proceedings.

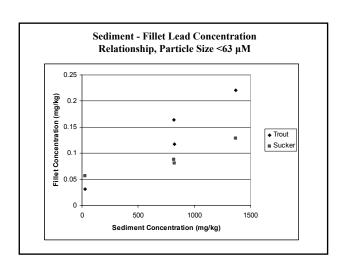


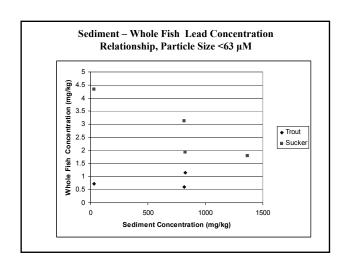
Relationship Between Particle Size and Sediment/Tissue Lead Concentration

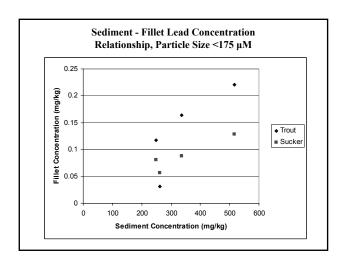
- Lead analyses done for particle size ranges of <63 μ M, <175 μ M, <500 μ M & <2000 μ M
- Avg. lead concentrations for each size range determined for sediment stations in the vicinity of fish sampling areas.
- Fillet/Whole fish vs. sediment lead concentrations plotted for different size ranges.

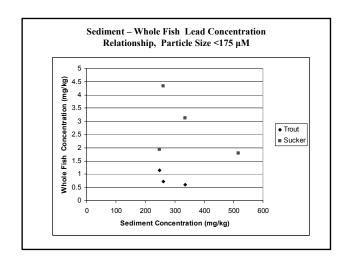
Sediment data compiled by Box and Wallis, USGS, 2000

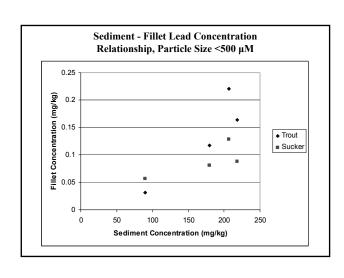


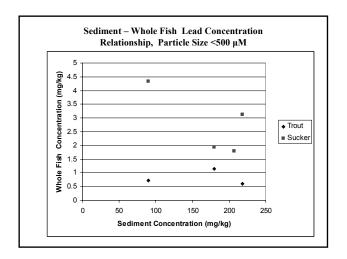


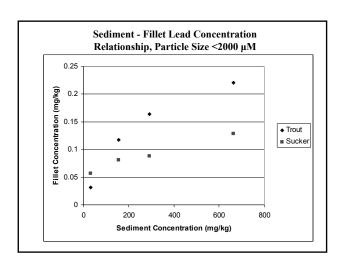


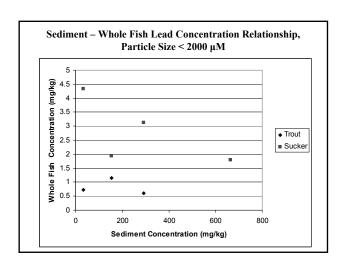


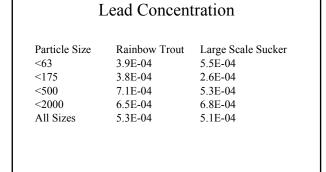












Ratio of Fillet Tissue to Sediment

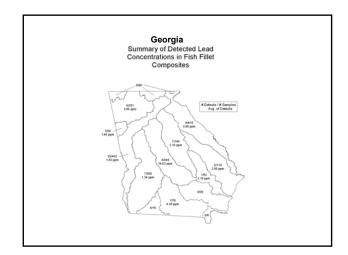
Comments on Use of Lead Tissue/Sediment Ratios

- Lead tissue/sediment ratios may be a useful method for screening as to whether or not fish consumption lead hazards exist.
- More work needs to be done to characterize these ratios.

Occurrence of Lead in Fish

Examples from Georgia, Maine, and California

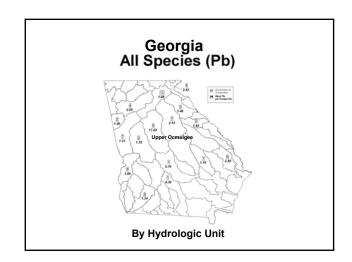
A Note on Contamination during Sample Preparation



Georgia Means of Detected Lead Values Only by Basin

	All Species		Largemouth Bass		Channel Catfish	
Basin	Composites	Mean	Composites	Mean	Composites	Mean
	(N)	Lead	(N)	Lead	(N)	Lead
		(ppm)		(ppm)		(ppm)
Altamaha	1	1.10	1	1.10		
Chattahoochee	25	1.52	4	1.98		
Coosa	4	2.05				
Flint	7	1.34	3	1.33	3	1.30
Ocmulgee	6	14.62	3	8.57	2	15.50
Oconee	7	2.16	2	2.55		
Ogeechee	6	2.50	1	2.50	1	2.50
Savannah	9	2.06	3	2.28		
Suwannee	1	4.30				
Tallapoosa	2	1.40				

Other detects in hogsuckers, trout and sunfish

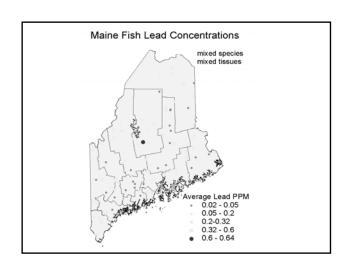


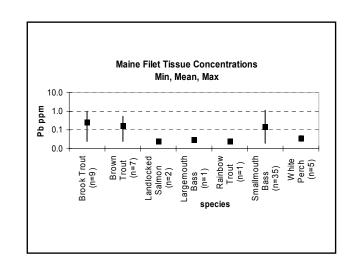
Georgia Largemouth Bass (Pb)

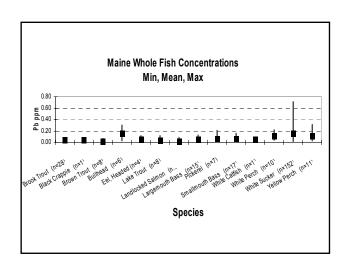


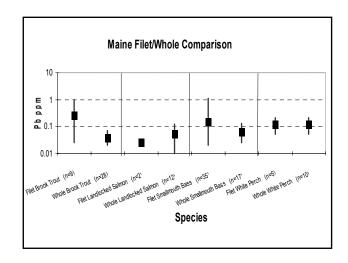
Georgia Channel Catfish (Pb)



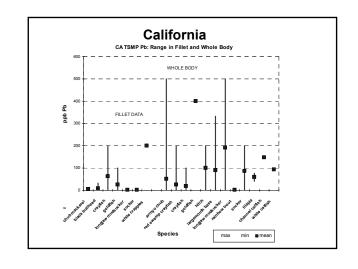








California Fillet Non-detects in TSMP Species Species Arroyo chub Lahonton cutthroat trout Largemouth bass Bluegill 4 7 Brook trout Mozambique tilapia Orangemouth Brown trout corvine Rainbow trout Carp Red swamp catfish Green crayfish Brown smoothhound sunfish shark Leopard shark Hitch



The Effects of Sample Preparation on Measured Concentrations of Eight Elements in Edible Tissues of Fish from Streams Contaminated by Lead Mining

Christopher Schmitt and Susan E. Finger Arch. Environ. Contam. Toxicol. 16, 185-207 (1987)

Effect of Preparation Method

Grand (seven sites) geometric mean concentration lead In ppm

Таха	Normal Prep	Clean Prep	Difference
Bass N=13	0.097	0.024	4X
Catfish N=13	0.314	0.031	10X
Redhorse N=14	0.228	0.220	equal

Redhorse sucker has intermuscular bones

Conclusions

- Preparation methods can effect reported Pb concentration
- Cross contamination from skin, bone, mucus and scales can effect reported
 Pb concentration
- Cross contamination and non-muscle fragments can effect sample heterogeniety

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